REMARKS

The Office Action of August 1, 2005 has been received and reviewed. Claims 1-17 are currently pending in the application. Claims 11, 12 and 14-16 were previously withdrawn from consideration. Claims 1-10, 13, 17 stand rejected. Claims 1-8 are amended herein. Claims 18 and 19 have been added. Claims 9, 10, 13 and 17 are cancelled herein. All claim amendments and cancellations are made without prejudice or disclaimer. No new matter has been added. Reconsideration of the application as amended herein is respectfully requested.

Priority

On October 14, 2005, applicants mailed a Certified Copy of the Priority Document 01200181.4 EP, filed January 18, 2001, in the European Patent Office. Applicants kindly request confirmation of receipt of the mailed priority document.

Specification

The specification was objected to because of the inclusion of an embedded hyperlink. As suggested by the Examiner, applicants have amended the specification at page 14, paragraph [0044], by deleting "http://" from the referenced internet address.

Claim objections

Claim 10 is objected to because it depends from a non-elected claim. Applicants have cancelled claim 10 making this objection moot.

Claim 13 is objected to because of an unintentional typographical error. Applicants have cancelled claim 13 making this objection moot.

Claims 3-7 and 9 are objected to as allegedly being of improper dependent form for failing to further limit the subject matter of a previous claim.

Regarding claims 3 and 4, applicants have amended these claims and removed any grounds for objection.

Regarding claims 5 and 6, applicants have amended these claims to be properly dependent from claim 1, thus removing any grounds for objection.

Applicants have amended claim 7 to remove any grounds for objection.

Finally, claim 9 has been cancelled making this objection moot.

For the foregoing reasons, applicants kindly request removal of the objections of claims 3-7, 9, 10 and 13 and reconsideration of the claims.

Claim Rejections—35 U.S.C. § 112, first paragraph, enablement

Claims 1-10, 13 and 17 are rejected under 35 U.S.C. § 112, first paragraph, because the specification allegedly fails to enable one of skill in the art to make and use the claimed invention. The Office Action states that the specification is enabling for providing candidate compounds, but allegedly fails to enable testing candidate compounds for their capacity to modulate or mimic binding of MCP-1 to L-CCR, or for identifying compounds that are candidates for treatment of all inflammatory diseases or all degenerative brain diseases.

While applicants do not agree with the alleged lack of enablement, applicants have amended independent claims 1 and 2 according to the Examiner's suggestions so that the method claims comprise the steps needed for detecting either the agonistic or antagonistic activity of a candidate drug compound. Moreover, the recited methods accomplish the goal stated in the preamble, thus removing any alleged need for undue experimentation to make or use the claimed invention.

Furthermore, amended claims 1 and 2 recite, in part, a method of *in vitro* detection of a chemokine receptor agonist/antagonist. In other words, the claims recite a method of identifying those candidate drug compounds that test positive as agonists or antagonists according the claimed method. However, as is to be expected, many of the agonists or antagonists detected by the claimed methods may not actually prove effective for treatment of disease. The Examiner states that there are no data to support the conclusion that an agent which mimics MCP-1 binding to the chemokine receptor L-CCR is a candidate for the treatment either inflammatory or degenerative brain diseases. (Office Action, page 6). However, the Examiner acknowledges that the specification correctly discloses that the MCP-1 binding to L-CCR induces chemotaxis and/or intracellular calcium and that exposure to LPS induces expression of the chemokine receptor L-CCR in cells which would make the cells more susceptible to the inflammatory chemotactic effects of MCP-1. Accordingly, the specification also correctly concludes that the use of antagonists or agonists of the chemokine receptor CCR12 would be useful in the treatment

of inflammatory or degenerative brain diseases. Therefore, those candidate drug compounds that, as recited in the amended claims 1 and 2, are chemokine receptor antagonists/agonists would be candidate drug compounds for the treatment of these diseases.

Additionally, the Office Action alleges that the induction of L-CCR or MCP-1 does not support a conclusion that MCP-1 binding to the chemokine receptor is a cause of inflammatory disease or degenerative brain disease. Applicants respectfully submit that there is no suggestion or speculation in the specification that the chemokine receptor is the cause of these diseases. The specification only makes a logical assumption and suggestion that when the L-CCR receptor is involved in these diseases, the candidate drug compounds that are agonists/antagonists of the receptors may be of therapeutic interests.

The Office Action also raised concerns that "the specification is not enabling for the discovery of agents which are reasonably construed as candidates for all inflammatory disease or all degenerative brain diseases." Applicants respectfully submit that amended claims 1 and 2 now recite, in part, a method of *in vitro* detection a chemokine receptor agonist/antagonist comprising providing a cell which expresses a chemokine receptor known as CCR12. Amended claims 1 and 2 do not recite "all inflammatory disease or all degenerative brain diseases" and, therefore, the specification is enabling for the scope of the claimed invention.

The specification also includes detailed instructions for the claimed invention. Paragraph [0045] contains detailed instruction for the determination of intercellular calcium and paragraph [0046] teaches a chemotaxis assay for detecting cell migration in response to chemokines.

The specification also includes working examples of the claimed invention that were created by following the instructions as described in the specification. Paragraph [0056] gives examples of the effects of chemokine receptor agonists MCP-1 and RANTES. Paragraph [0057] provides further examples of chemotaxis of chemokine receptor CCR12 expressing cells in response to an agonist gradient. Additionally, paragraph [0058] shows the *in vitro* effects of the chemokines receptor agonist MCP-1 on the chemotaxis and cellular calcium of cultured cells.

For the foregoing reasons, applicants submit that the specification enables on of skill in the art to make and used the claimed invention without undue experimentation. Accordingly, applicants respectfully request removal of the rejection and reconsideration of the rejected claims.

Claim Rejections—35 U.S.C. § 112, first paragraph, written description

Claims 1-10, 13 and 17 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter allegedly not described in the specification in sufficient detail to convey to one of skill in the art that the inventors had possession of the claimed invention at the time of filing. The Examiner alleges that applicants have failed to describe compounds that modulate or mimic the binding of MCP-1 to L-CCR or CRAM-B.

Applicants wish to note that claims 9, 10, 13 and 17 have been cancelled making the rejection moot as to these claims. In regards to the remaining rejected claims, including independent claims 1 and 2, and those dependent therefrom, applicants submit that the amendments herein remove any grounds for rejection.

More particularly, amended claims 1 and 2 recite, in part, a method of *in vitro* detection of a chemokine receptor agonist/antagonist comprising providing a cell which expresses a chemokine receptor known as CCR12 and providing a candidate drug compound to the cell; and checking if the candidate drug compound is a chemokine receptor agonist/antagonist by measuring chemotaxis of the cells towards the candidate drug compound or by measuring intracellular calcium gradients.

As discussed previously, the specification contains detailed examples and instructions for the claimed invention. Furthermore, the claimed methods recite active steps which accomplish the goals of the preamble. Therefore, the skilled artisan, reading the specification, would be able to envision how to carry out the claimed methods.

As such, applicants submit that the specification contains sufficient examples and detailed instructions to reasonably convey to one of skill in the art that the inventors had possession of the claimed invention at the time of filing. Applicants respectfully request removal of the rejection and reconsideration of the claims.

Claim Rejections—35 U.S.C. § 112, second paragraph

Claims 1-10, 13 and 17 are rejected under 35 U.S.C. § 112, second paragraph, as being incomplete as allegedly omitting the essential elements of the MCP-1 and L-CCR proteins.

Claims 9, 10, 13 and 17 have been cancelled making the rejection moot as to these

claims. Furthermore, the amendments herein to independent claims 1 and 2 and those claims dependent therefrom, remove any grounds for rejection and do not omit any essential elements of the claims.

Therefore, applicants respectfully request removal of the rejection and reconsideration of the claims.

Claims 1-10, 13 and 17 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. Again, applicants note that claims 9, 10, 13 and 17 have been cancelled making the rejection moot as to these claims.

Moreover, applicants respectfully submit that the amended claims 1 and 2, and those dependent therefrom, have removed any alleged indefiniteness and, therefore, allow a skilled artisan to determine the metes and bounds of the claims. As such, applicants kindly request removal of the rejection and reconsideration of the claims.

Claim rejections—35 U.S.C. § 102

Claims 1-2, 7-9 and 13 are rejected under 35 U.S.C. § 102 (b) as being anticipated by Schweickart *et al.* Claims 9 and 13 have been cancelled herein thus mooting the rejection for these claims. Applicants respectfully assert that Schweickart fails to disclose each and every element of the rejected claims.

Amended claims 1 and 2 of the claimed invention recite, in part, a method of *in vitro* detection of a chemokine receptor agonist/antagonist comprising **providing a cell which expresses a chemokine receptor known as CCR12**. CCR12 is the name of a orphan mouse chemokine receptor. Paragraph [0013] of the instant specification discloses that a paired nucleotide sequence alignment of CCR12 with all other known mouse CC chemokine receptors (CCR1-10 and D6) confirms that CCR12 encodes a new chemokine receptor.

Schweickart teaches the isolation of a human homologue of an orphan bovine chemokine receptor PPR1 which was and named CCR11 in accordance with the Chemokine Nomenclature Committee. (*See* Schweickart *et al.*, page 9950, column 2). Therefore, Schweickart fails to teach, directly or inherently, each and every element of the rejected claim. As such, applicants kindly request removal of this rejection and request reconsideration of the

claims.

Claims 1-2, 7-10 and 13 are rejected under 102(e) as being anticipated by Gray *et al.* Claims 9, 10 and 13 have been cancelled herein making this rejection moot as to these claims. Applicants respectfully traverse this rejection because Gray *et al.* fails to expressly or inherently disclose every limitation of the rejected claims.

Amended claims 1 and 2 of the claimed invention recite, in part, a method of *in vitro* detection of a chemokine receptor agonist/antagonist comprising **providing a cell which expresses a chemokine receptor known as CCR12**. CCR12 is the name of a orphan mouse chemokine receptor. As discussed previously, paragraph [0013] of the instant specification discloses that a paired nucleotide sequence alignment of CCR12 with all other known mouse CC chemokine receptors (CCR1-10 and D6) confirms that CCR12 encodes a new chemokine receptor.

In contrast, Gray teaches assays to identify modulators of CCR11—the human homolog of a orphan bovine chemokine receptor identified originally as PPR1 in bovine papillary tissue, and named CCR11 in accordance with the Chemokine Nomenclature Committee. (Gray *et al.*, Example 1; *See* Schweickart *et al.*, page 9950, column 2). Therefore, Gray *et al.* fails to disclose inherently or expressly each and every element of amended claims 1 or 2. As such, applicants kindly request removal of this rejection and request reconsideration of the claims.

Claims 1-2 and 13 are rejected under 35 U.S.C. § 102 (b) as being anticipated by Gish *et al.* Claim 13 has been cancelled herein thus mooting the rejection of this claim. Applicants respectfully traverse this rejection because Gish *et al.* fails to expressly or inherently disclose every limitation of amended claims 1 and 2.

More particularly, claims 1 and 2 recite, in part, a method of *in vitro* detection of a chemokine receptor agonist/antagonist comprising **providing a cell which expresses a chemokine receptor known as CCR12** and providing a candidate drug compound to the cell; and checking if the candidate drug compound is a chemokine receptor agonist/antagonist by measuring chemotaxis of the cells towards the candidate drug compound or by measuring

intracellular calcium gradients.

Gish *et al.* does not teach a method of *in vitro* detection of a chemokine receptor agonist or antagonist, the method comprising providing a cell which expresses a chemokine receptor known as CCR12. Therefore, Gish *et al.* fails to expressly or inherently disclose each element of amended claims 1 and 2, and those dependent therefrom. Accordingly, applicants respectfully request removal of the rejection and reconsideration of the claims.

Claims 1, 2, 8 and 13 are rejected under 35 U.S.C. 102 (b) as being anticipated by Boddeke *et al.* as evidenced by Dorf and by Schweickart. Claim 13 has been cancelled herein making the rejection moot as to this claim. Applicants respectfully traverse this rejection as every element of the rejected claims is not found in a **single prior art reference**.

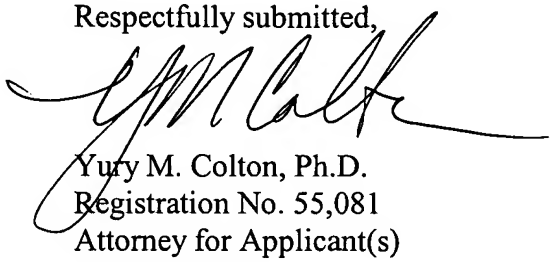
More particularly, amended independent claims 1 and 2 recite, in part, a method of *in vitro* detection of a chemokine receptor agonist/antagonist comprising providing a cell which expresses a chemokine receptor known as CCR12 and providing a candidate drug compound to the cell; and detecting if the candidate drug compound is a chemokine receptor agonist/antagonist by **measuring chemotaxis of the cells** towards the candidate drug compound or by measuring intracellular calcium gradients.

Boddeke *et al.* fails to expressly or inherently teach all the elements of amended claims 1 and 2, and those dependent therefrom, including the detection of a chemokine receptor agonist/antagonist by measuring the chemotaxis of the cells toward a candidate drug compound. Accordingly, applicants respectfully request removal of the rejection and reconsideration of the claims.

CONCLUSION

In view of the foregoing amendments and remarks, the applicants submit that the claims define patentable subject matter and a notice of allowance is requested. Should questions exist after consideration of the foregoing, the Office is kindly requested to contact the applicants' attorney at the address or telephone number given herein.

Respectfully submitted,



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